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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,319		Hidetoshi Uemura	UEMURA 5	6685

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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	PAPER NUMBER
1636	23

DATE MAILED: 07/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,319	UEMURA ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33 and 35-43* is/are pending in the application.

4a) Of the above claim(s) *11-19,27-31,35-37,40 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-26,32,33,38,39,42,43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 May 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *20* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Office Action is a response to the "Reply: Amendment and Remarks" filed 5/8/03 (Paper No. 22) in response to the Non-Final Office Action mailed 8 January 2003 (Paper No. 18). Claims 11-19, 27-31, 35-37, 40 and 41 were withdrawn from consideration and claims 20-26, 32, 33, 38, 39, 42 and 43 were considered in paper No. 18. Claims 20, 22-25, 32, 33, 42 and 43 were amended in Paper No. 18. Claims 1-33 and 35-43 are pending and claims 20-26, 32, 33, 38, 39, 42 and 43 are under consideration.

Election/Restrictions

In response to the arguments set forth in Paper No. 18, Applicant reiterates the argument that Group III shares a common special technical feature with claim 35 (Group II) because the claims depend from and incorporate the subject matter of claim 35. As pointed out in the previous Office Action, because claim 35 is directed to an enzyme while the claims of Group III are directed to antibodies, Group III incorporates the subject matter of Claim 35 only to the extent that the claim limits the range of proteins to which the antibody can bind. Neither the structural nor the functional limitations of the enzyme of claim 35 are incorporated into the claims of Group II, as a protein having the structure and function of the enzyme to which claim 35 is directed would not function as an antibody. Therefore, the proteins embraced by Groups I and II are both structurally and functionally distinct and thus do not share a special technical feature. Therefore, the finality of the restriction requirement stands.

This application contains claims 11-19, 27-31, 35-37, 40 and 41 drawn to an invention nonelected with traverse in Paper No. 17. A complete reply to the final rejection must include

cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Response to Amendment

Specification

Objection to the title is withdrawn.

Claim Rejections - 35 USC § 101

Rejection of claims 20 and 21 under 35 U.S.C. 101 as directed to non-statutory subject matter is withdrawn.

Claim Rejections - 35 USC § 112

Claims 20-26, 32, 33, 38, 39, 42 and 43 stand rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description for reasons of record in Paper No. 18 and herein below in the response to arguments.

Claims 20-26, 32, 33, 38, 39, 42 and 43 stand rejected under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter for reasons of record in Paper No. 18 and herein below in the response to arguments.

Rejection of claims 20-26, 32, 33, 38, 39, 42 and 43 under 35 U.S.C. 112, second paragraph, as indefinite is withdrawn in view of the amendments to the claims and clarification provided in Paper No. 22.

Claim Rejections - 35 USC § 102

Claims 20, 21, 23, 24, 26 and 38 stand rejected under 35 U.S.C. 102(b) as anticipated by Carrere *et al.* (1986) *Biochim. Biophys. Acta* 883:46-53 for reasons of record in Paper No. 18 and herein below in the response to arguments.

Claims 20, 21, 23, 25, 26 and 39 stand rejected under 35 U.S.C. 102(b) as anticipated by Geokas *et al.* (1979) *J. Biol. Chem.* 254:2775-2781 for reasons of record in Paper No. 18 and herein below in the response to arguments.

Claims 20-23, 42 and 43 stand rejected under 35 U.S.C. 102(b) as anticipated by Chu *et al.* (1984; U.S. Patent No. 4,446,122) for reasons of record in Paper No. 18 and herein below in the response to arguments.

Claims 20, 21, 23, 25, 26, 32, 33, 39 and 42 stand rejected under 35 U.S.C. 102(b) as anticipated by Iwaki *et al.* (1983) *Res. Commun. Chem. Pathol. Pharmacol.* 40:489-496 for reasons of record in Paper No. 18 and herein below in the response to arguments.

Claim Rejections - 35 USC § 103

Rejection of claims 33 and 42 rejected under 35 U.S.C. 103(a) as unpatentable over Lesi *et al.* (1984) *Digestion* 30:114-115 in view of Carrere *et al.* *(supra)* is withdrawn in view of the limitation of the claims to detecting the protein in a tissue specimen.

Response to Arguments

Claim Rejections - 35 USC § 112

In response to rejection of claims 20-26, 32, 33, 38, 39, 42 and 43 under 35 U.S.C. 112, first paragraph, as lacking adequate written description, Applicant has amended the claims such that they are now limited to an antibody against a protein comprising the amino acid sequence of residues 1-231 of SEQ ID NO: 2 or SEQ ID NO: 4 or a protein encoded by a nucleotide sequence that hybridizes to a nucleotide sequence complementary to nucleotides 110-802 of SEQ ID NO: 1 or nucleotides 132-824 of SEQ ID NO: 3, wherein the protein has serine protease activity. Applicant argues that the amendments obviate the rejection.

Upon careful consideration of the amended claims, it is clear that disclosure still fails to provide adequate written description for the full scope of the claimed subject matter. As stated in the previous Office Action, "only the described antibodies that bind to the sequences set forth as SEQ ID NO: 2 and 4 meet the written description provision of 35 U.S.C. §112, first paragraph" (page 8). First, as the claims are directed to an antibody against a protein that comprises the disclosed amino acid sequence, the polypeptide sequence to which the claimed antibody can bind is still essentially unlimited. That is, because the antibody is not limited to recognizing the disclosed amino acid sequence and any protein can be fused to the disclosed amino acid sequence to produce a polypeptide comprising the disclosed amino acid sequence, the claims encompass an antibody against any polypeptide. The claims are therefore clearly directed to antibodies that bind polypeptides that are not described in the specification. Amending the claims

such that "consisting of" is substituted for "comprising" would obviate these grounds for rejection.

The disclosure also fails to provide adequate written description for the genus of antibodies encompassed by antibodies against a protein encoded by a nucleotide sequence that hybridizes to a nucleotide sequence complementary to nucleotides 110-802 of SEQ ID NO: 1 or nucleotides 132-824 of SEQ ID NO: 3. Although the claim specifies that hybridization occur under "stringent" conditions, the specification provides, at pages 20-21, only a non-limiting example of stringent hybridization conditions. Thus, "stringent" conditions encompass any stringency, even very low stringency conditions, which would result in hybridization of the disclosed nucleic acids with nucleic acids having only very limited structural similarity to SEQ ID NO: 1 or 3. Furthermore, the conditions set forth in the specification (i.e., 2X SSC, 0.1% SDS, room temperature) are considered low stringency and would allow hybridization to nucleic acids having very limited structural similarity to the probe sequence. Therefore, even claims limited by the hybridization conditions set forth in the specification encompass a broadly divergent genus of antibodies, which, for reasons set forth in Paper No. 18, lack adequate written description. Therefore, the claims stand rejected under 35 U.S.C. §112, first paragraph.

In response to rejection of claims 20-26, 32, 33, 38, 39, 42 and 43 under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter, Applicant has amended the claims as described above. Applicant argues that the scope of the claimed subject matter, as it is now limited, is fully enabled by the specification. However, for reasons set

forth above regarding written description of the claimed subject matter, the claims still encompass antibodies for which the specification fails to provide an enabled use.

With regard to enablement of claims directed to diagnosing Alzheimer's disease or cancer, Applicant points to teachings in the specification which Applicant states, "[describe] how other kinds of serine proteases may be used for detecting or diagnosing Alzheimer's disease" and "describes other kinds of serine proteases used in the detection or diagnosis of cancer" (page 16). Applicant also points to teachings in the specification which reveal sites where the serine proteases of the present invention are expressed.

These arguments have been fully considered but are not found persuasive. With regard to Alzheimer's disease, the teaching cited by Applicant is merely a statement that serine proteases are expressed in the nervous system and a general discussion of the need for a diagnostic marker for Alzheimer's disease and the inadequacy of presently available markers. There is nothing in these teachings that would suggest any correlation of the disclosed protein to Alzheimer's pathology that would enable the skilled artisan to use the claimed antibody to diagnose Alzheimer's disease. Applicant's statement that other kinds of serine proteases may be used for detecting or diagnosing Alzheimer's disease seems to argue that the claims are enabled because some other serine protease not contemplated in the specification might be involved in Alzheimer's disease. Clearly this is not the case because it requires that the skilled artisan must identify the relevant serine protease without any guidance from the disclosure as to the identity of that serine protease. Therefore, the skilled artisan would obviously have to engage in undue empirical experimentation in order to practice the claimed invention.

With regard to diagnosis of cancer, as pointed out in the previous Office Action, "neither the specification nor the prior art teaches that the presence or absence of the proteins disclosed in the instant application is in any way associated with any known cancer, let alone all cancers to which the claims are directed" (bridging pages 10-11). Applicant's argument that other kinds of serine proteases can be used in the detection or diagnosis of cancer is not persuasive. As above, the specification provides no guidance as to which serine proteases can be used to diagnose cancer and therefore the skilled artisan must identify the relevant serine protease without any guidance from the disclosure. Furthermore, the specification provides no guidance as to which cancers might be diagnosed by the method of detecting a serine protease, and therefore the skilled artisan would have to engage in undue experimentation to identify the types of cancers that could be diagnosed according to the claimed method. Clearly this would require undue experimentation; therefore the claims fail to meet the enablement requirement of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

In response to rejection of claims 20, 21, 23, 24, 26 and 38 as anticipated by Carrere *et al.*; claims 20, 21, 23, 25, 26 and 39 as anticipated by Geokas *et al.*; claims 20-23, 42 and 43 as anticipated by Chu *et al.*; and claims 20, 21, 23, 25, 26, 32, 33, 39 and 42 as anticipated by Iwaki *et al.*, Applicant argues that the amended claims are no longer anticipated by the art because the claims no longer encompass an antibody against any protein. However, for reasons set forth above with regard to the written description rejection, the antibody of the claims still encompasses an antibody against any protein having serine protease activity. Therefore, the

instant products and methods still encompass the products and methods taught in the cited art and the claims stand rejected as anticipated by Carrere *et al.*, Geokas *et al.*, Chu *et al.* and Iwaki *et al.*

New Grounds

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 21, 23, 24, 25, 26, 33, 38 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Reseland *et al.* (1997) *J. Biol. Chem.* 272:8099-8304 (made of record in the IDS filed 9 April 2003.

Reseland *et al.* teaches an antibody against human chymotrypsin-like serine protease and a composition comprising said antibody, which is encompassed by claims 20, 21 and 33 as they are directed to an antibody against any protein and a composition comprising said antibody (see especially the paragraph bridging pages 8100-8101 and Figure 4 and the caption thereto). In the second full paragraph on page 8101, Reseland *et al.* teaches a method for determining a protein, or modified derivative or fragment thereof, comprising detecting said protein with an antibody according to the methods of claims 23-25. The method of Reseland *et al.* further comprises a specimen that is a body fluid (i.e., pancreatic secretions) according to claims 26, 38 and 39 (see especially the caption to Figure 4).

The antibody, composition and method taught by Iwaki *et al.* are the same as those taught in the instant application; therefore the limitations of the claims are met by Iwaki *et al.*

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Reseland *et al.* (1997) *J. Biol. Chem.* 272:8099-8304 as applied to claim 21 above and in view of "Chapter 6: Monoclonal Antibodies" *in* Antibodies: a laboratory manual (Harlow and Lane eds.), Cold Spring Harbor Laboratory, 188, pages 139-149 (hereinafter Antibodies).

The claim is directed to a method of producing a monoclonal antibody having the properties first set forth in claim 21. As described herein above, Reseland *et al.* teaches an

antibody having the properties of the antibody of claim 21. Reseland *et al.* does not teach production of a monoclonal antibody. The process steps for making a monoclonal antibody are routine in the art and are set forth in detail in Antibodies (see Figure 6.3, page 149, for an overview).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to modify the teachings of Reseland *et al.* to include the teachings set forth in Antibodies to produce a monoclonal antibody according to the limitations of the instant claim 22. Motivation to combine these teachings comes from Antibodies, which teaches that monoclonal antibodies have a number of advantages (see the section entitled "Monoclonal antibodies are powerful immunochemical tools" bridging pages 141 and 142). Absent evidence to the contrary, one would have a reasonable expectation of success in combining these teachings because the production of monoclonal antibodies from a source of polyclonal antibodies is routine in the art.

Conclusion

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 9 April 2003 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms
July 22, 2003

JAMES KETTER
PRIMARY EXAMINER